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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,509	03/31/2004	Anthony E. Bolton	355908-3951	8220

38706 7590 11/15/2006

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EXAMINER	
ARNOLD, ERNST V	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 11/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/815,509	BOLTON ET AL.	
	Examiner	Art Unit	
	Ernst V. Arnold	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-22 are pending in the application. Claims 21 and 22 have been withdrawn from consideration as being drawn to non-elected subject matter.

The Examiner acknowledges Applicant's remarks filed on 8/8/06. The Examiner further acknowledges the declaration of Dr. Eldon Raymond Smith filed on 8/14/06. Dr. Smith clearly distinguishes primary pulmonary hypertension from secondary pulmonary hypertension thus establishing that they are two different diseases. Upon further consideration the Examiner has a new ground of rejection. This action is non-final.

Withdrawn rejections/objections:

Claims 1-20 were rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (US 2002/0051766) in view of Sakai et al. (JACC 1996, 28(6), 1580-1588) and Cooke et al. (International Angiology 1997, 16(4), 250-254). The declaration by Dr. Smith clearly distinguishes primary pulmonary hypertension form other forms of pulmonary hypertension. In addition, Applicant asserted that the cited references do not teach treatment of primary pulmonary hypertension because the pulmonary hypertension taught by the references is caused by congestive heart failure and thus not primary pulmonary hypertension, which has an unknown etiology. The Examiner agrees and withdraws the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treatment according the present invention on endothelin levels in the LDL receptor (LDL-R) deficient mouse model, a widely used transgenic atherosclerosis model created by targeted disruption of the LDL receptor, does not reasonably provide enablement for preventing primary pulmonary hypertension. Please note that the Examiner is interpreting prophylaxis to mean prevention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims without an undue amount of experimentation.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: 1) scope or breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are

weighed, it is the Examiner's position that one skilled in the art could not practice the invention without undue experimentation.

1) Scope or breadth of the claims

The claims are broader in scope than the enabling disclosure. The specification merely discloses, without more, that a method for treatment according the present invention on endothelin levels in the LDL receptor (LDL-R) deficient mouse model, a widely used transgenic atherosclerosis model created by targeted disruption of the LDL receptor (page 10, example 1). However, Applicant is purporting to prevent primary pulmonary hypertension.

2) Nature of the invention

The nature of the invention is directed to a method for treatment according the present invention on endothelin levels in the LDL receptor (LDL-R) deficient mouse model, a widely used transgenic atherosclerosis model created by targeted disruption of the LDL receptor.

3) Relative level of skill possessed by one of ordinary skill in the art

The relative level of skill possessed by one of ordinary skill in the art of medical research is relatively high, as a majority of lead investigators conducting scientific research and development in this particular technological area possess an M.D. and/or a Ph.D. in a scientific discipline such as organic synthetic chemistry, medicinal chemistry, biochemistry, pharmacology, biology or the like.

4) State of, or the amount of knowledge in, the prior art

The art teaches that goal of treatment for primary pulmonary hypertension is control of the symptoms (Medical Encyclopedia: Primary pulmonary hypertension).

5) Level or degree of predictability, or a lack thereof, in the art

A high degree of unpredictability existed in the state of the prior art regarding how to cure primary pulmonary hypertension. There is no cure for primary pulmonary hypertension and the cause of primary pulmonary hypertension is unknown (Medical Encylopedia: Primary pulmonary hypertension; causes, incidence and risk factors; treatment). The declaration by Dr. Smith states that "treatments proven effective in secondary pulmonary hypertension are not effective in (and occasionally may worsen) primary pulmonary hypertension."

6) Amount of guidance or direction provided by the inventor

Applicant was required to provide in the specification additional guidance and direction with respect to how use the claimed subject matter in order for the application to be enabled with respect to the full scope of the claimed invention. Although the instant specification discloses a method for treatment according the present invention on endothelin levels in the LDL receptor (LDL-R) deficient mouse model, a widely used transgenic atherosclerosis model created by targeted disruption of the LDL receptor, it does not reasonably provide enablement for preventing primary pulmonary hypertension.

7) Presence or absence of working examples

The specification fails to provide scientific data and working embodiments with respect to a method for preventing primary pulmonary hypertension.

8) Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure

One of ordinary skill in the art is then faced with the daunting task of treating individuals with a disease without a known cause and where there is no known cure in an effort to prevent the disease. This is especially difficult when some of the cases may be caused by a genetic defect

(Medical Encylopedia: Primary pulmonary hypertension; causes, incidence and risk factors). As a result, one of ordinary skill in the art would be required to conduct an undue amount of experimentation to reasonably and accurately determine whether the method can prevent primary pulmonary hypertension in each and every case.

Claim Rejections - 35 USC § 112

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treatment according the present invention on endothelin levels in the LDL receptor (LDL-R) deficient mouse model, a widely used transgenic atherosclerosis model created by targeted disruption of the LDL receptor, by extracting an aliquot of blood from the patient, subjecting the aliquot extacorporeally to at least two stressors selected from the group consisting of a temperature above or below body temperature in the range of about -5 C to about 55 C, an electromagnetic emission comprising UV light and an oxidative environment comprising ozone/oxygen gas mixture for a time period up to about 60 minutes, does not reasonably provide enablement for a method for alleviating the symptoms of primary pulmonary hypertension by extracting an aliquot of blood from the patient, subjecting the aliquot extacorporeally to at least two stressors selected from the group consisting of a temperature above or below body temperature, an electromagnetic emission comprising UV light and an oxidative environment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims without an undue amount of experimentation.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: 1) scope or breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the invention without undue experimentation.

1) Scope or breadth of the claims

The claims are broader in scope than the enabling disclosure. The specification merely discloses, without more, that a method of treatment according the present invention on endothelin levels in the LDL receptor (LDL-R) deficient mouse model, a widely used transgenic atherosclerosis model created by targeted disruption of the LDL receptor (Page 10, example 1), consisting of a temperature above or below body temperature in the range of about -5 C to about 55 C, an electromagnetic emission comprising UV light and an oxidative environment comprising ozone/oxygen gas mixture for a time period up to about 60 minutes,. However, Applicant is purporting to a method for alleviating the symptoms of primary pulmonary hypertension by extracting an aliquot of blood from the patient, subjecting the aliquot extacorporeally to at least two stressors selected from the group consisting of a temperature

above or below body temperature, an electromagnetic emission comprising UV light and an oxidative environment.

2) Nature of the invention

The nature of the invention is directed to a method of alleviating the symptoms of primary pulmonary hypertension.

3) Relative level of skill possessed by one of ordinary skill in the art

The relative level of skill possessed by one of ordinary skill in the art of medical research is relatively high, as a majority of lead investigators conducting scientific research and development in this particular technological area possess an M.D. and/or a Ph.D. in a scientific discipline such as organic synthetic chemistry, medicinal chemistry, biochemistry, pharmacology, biology or the like.

4) State of, or the amount of knowledge in, the prior art

The art teaches that goal of treatment for primary pulmonary hypertension is control of the symptoms (Medical Encyclopedia: Primary pulmonary hypertension).

5) Level or degree of predictability, or a lack thereof, in the art

A high degree of unpredictability existed in the state of the prior art regarding how to cure primary pulmonary hypertension. There is no cure for primary pulmonary hypertension and the cause of primary pulmonary hypertension is unknown (Medical Encylopedia: Primary pulmonary hypertension; causes, incidence and risk factors; treatment).

6) Amount of guidance or direction provided by the inventor

Applicant was required to provide in the specification additional guidance and direction with respect to how use the claimed subject matter in order for the application to be enabled with

respect to the full scope of the claimed invention. Although the instant specification discloses a method for treatment according the present invention on endothelin levels in the LDL receptor (LDL-R) deficient mouse model, a widely used transgenic atherosclerosis model created by targeted disruption of the LDL receptor, does not reasonably provide enablement for treatment of primary pulmonary hypertension with all temperatures above or below body temperature (would the temperature of liquid nitrogen work?), all electromagnetic emissions (would radio waves, microwaves, infrared radiation, visible light, X-rays and gamma rays work?) and all oxidative environments (would air or hydrogen peroxide solutions work?).

7) Presence or absence of working examples

The specification fails to provide scientific data and working embodiments with respect to a method for treating primary pulmonary hypertension with all temperatures above or below body temperature, all electromagnetic emissions and all oxidative environments. Applicant has not supplied one example of treating a patient with primary pulmonary hypertension with the instantly claimed method.

8) Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure

One of ordinary skill in the art is then faced with the daunting task of treating individuals with a disease without a known cause and where there is no known cure in an effort to prevent the disease with a myriad number of combinations of stressors without any guidance from the instant specification. For example would gamma ray irradiation followed by hydrogen peroxide solution treatment at 100 C work? This is especially difficult when one of ordinary skill in the art knows that failure can hasten the patient's demise. Even Dr. Smith acknowledges that

treatments that have proven effective in secondary pulmonary hypertension are not effective in primary pulmonary hypertension. Thus in a disease that is acknowledged by experts to be difficult to treat, how can one skilled in the art accept the broad assertions of treating primary pulmonary hypertension without significant data to support such a statement? As a result, one of ordinary skill in the art would be required to conduct an undue amount of experimentation to reasonably and accurately determine whether the method can work for treating primary pulmonary hypertension with all temperatures above or below body temperature, all electromagnetic emissions and all oxidative environments. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Conclusion

No claims are allowed..

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (6:15 am-3:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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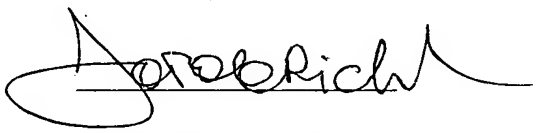

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